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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/533,559 | 03/22/2000 | Randy M. Berka | 5849.200-US | 6980 |

25907 7590 02/25/2002

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EXAMINER

BRUSCA, JOHN S

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1631

DATE MAILED: 02/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/533,559

Applicant(s)

BERKA ET AL.

Examiner

Brusca S John

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 22 March 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 11-13, 19, 20, 26-28, 34, 40-42, 62, 64 and 65 is/are pending in the application.
- 4a) Of the above claim(s) 3-5, 12, 13, 26-28, 41, 42, 62, 64 and 65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 11, 19, 20, 34 and 40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other _____

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 1. Claims 1-5, 11-13, 19, 20, 26-28, 34, and 40, drawn to a method of differential gene expression analysis, classified in class 435, subclass 6.
 2. Claims 41, 42, and 62 drawn to computer readable media comprising data, classified in class 365, subclass 94.
 3. Claims 64 and 65, drawn to arrays of polynucleotides, classified in class 536, subclass 24.32

The inventions are distinct, each from the other because of the following reasons:

Inventions 1 and 2 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the method of Invention 1 does not utilize the computer readable memory of Invention 2.

Inventions 3 and 1 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the array of ESTs of Invention 3 could be used to determine the presence of a genomic sequence rather than the level of expression of a genomic sequence as in the method of Invention 1.

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Inventions 2 and 3 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to two different compositions, one an array of polynucleotides, and the other a computer readable medium comprising data of sequence information.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

2. This application contains claims directed to the following patentably distinct species of the claimed invention:

For Invention 1: The first level of species are those enumerated as different genera of filamentous fungi in claims 2, 3, 4, 5, 11-13, 19, 20, 26-28, or 34. In addition, a second level of subspecies election is required of a single combination of the alternative combinations of sequences listed in claims 13, 20, or 28, should an applicable genus of filamentous fungi be elected in the first level of species detailed above. Note that a single combination of sequences is required to be elected as detailed in Example C in MPEP 803.04.

For Invention 2: The species are the alternative genera of filamentous fungi listed in claim 42.

For Invention 3: The species are the alternative genera of filamentous fungi listed in claim 65

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally

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held to be allowable. Currently, claims 1, 34, and 40 are generic and claim 2 is a Markush-type claim in Invention 1, claims 41 and 62 are generic and claim 42 is a Markush-type claim in Invention 2, and claim 64 is generic and claim 65 is a Markush-type claim in Invention 3.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

3. During a telephone conversation with Robert Stearns on 24 January 2002 a provisional election was made with traverse to prosecute the invention of Invention 1, claims 1, 2, 34, 40, and the species *Aspergillus oryzae* EST combination of SEQ ID NOS:4377-7401 to which claims 11, 19, and 20 are drawn in increasing specificity, respectively. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3-5, 12, 13, 26-28,

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41, 42, 62, 64, and 65 are withdrawn from further consideration by the examiner, 37

CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC 101 and 112

4. Definitions: [from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from <http://www.uspto.gov/web/menu/utility.pdf>]

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

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- A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.
- B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. ' 101.)
- C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".
- D. A method of making a material that itself has no specific, substantial, and credible utility.
- E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, if a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

A "Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

See also the MPEP at 2107 - 2107.02.

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 20 is rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The claimed combination of nucleic acids is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. The disclosed utility is to use an array of *Aspergillus oryzae* ESTs to determine expression profiles that are correlated with different types of cells or different growth states of cells. No evidence has been disclosed that the elected SEQ ID NOS allow for determination of the state or type of cell that is assayed

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by the claimed method of using an array of *Aspergillus oryzae* ESTs. Further research is required to determine whether the claimed method utilizes ESTs that allow for useful discrimination between cell types or cell states. The research required to establish the utility of the claimed method is not consistent with a substantial utility. Identifying and studying the properties of an array of ESTs does not define a "real world" context or use. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the array of ESTs such that another non-asserted utility would be well established for the compounds.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 20 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a substantial utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses SEQ ID NO: 4377-7401. SEQ ID NO: 4377-7401 meets the written description provisions of 35 USC 112, first paragraph. However, because it is not apparent that SEQ ID NO: 4377-7401 comprises a complete open reading frame, claim 20 is directed to encompass gene sequences and complete cDNA sequences due to the recitation of the

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phrase "and nucleic acid sequences having at least 90% homology to SEQ ID NOS: 4377-7401." The claims further encompass sequences that hybridize or are similar to SEQ ID NO: 4377-7401, corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 4377-7401, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

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Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

Therefore, only SEQ ID NO: 4377-7401 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 2, 11, 19, 20, 34, and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 11, 19, 20, 34, and 40 are indefinite for recitation in claim 1 part (b) (i) of the phrase "the ESTs...produce a distinct first fluorescence emission color" and further in part (b)

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(ii) of the phrase "the ESTs in the array...produce a distinct combined fluorescence emission color" because it is not clear from the claims whether the fluorescence is produced by the fluorescence-labeled nucleic acids or by the ESTs. The rejection would be overcome by amending claim 1 to recite in claim 1 part (b) (i) the phrase "the fluorescence-labeled nucleic acids obtained from either the first or the one or more second filamentous fungal cells that are hybridized to the ESTs in the array produce a distinct first fluorescence emission color" and further in part (b) (ii) the phrase "the fluorescence-labeled nucleic acids obtained from both the first and one or more second filamentous fungal cells that are hybridized to the ESTs in the array produce a distinct combined fluorescence emission color."

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over DeRisi et al. in view of Machida et al. in view of Minetoki et al. in view of Hata et al.

The claim is drawn to a method of analyzing two different samples of *Aspergillus oryzae* nucleic acids that are labeled by different fluorophores by use of an array of *Aspergillus oryzae* ESTs.

DeRisi et al. shows in the abstract and throughout the use of an array of *Saccharomyces cerevisiae* to measure the level of mRNA in *Saccharomyces cerevisiae* grown at different growth conditions by synthesizing cDNA from mRNA of cells grown in the different conditions. DeRisi et al. show throughout that the analysis of the changes in the expression profiles for the sequences tested by the array can be used to gain insights into the metabolism of the tested cells.

Michida et al. shows on pages 427-428 and Figure 5 the measurement of the steady state levels of *Aspergillus oryzae* enolase mRNA after growth in different carbon sources.

Minetoki et al. shows on page 1519 and Table 2 the measurement of the activity of *Aspergillus oryzae* alpha-glucosidase gene after growth in different carbon sources, and further state on page 1520 that the regulation is at the transcriptional level.

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Huta et al. shows on page 86 and Figure 1 the measurement of the steady state levels of *Aspergillus oryzae* glucoamylase mRNA after growth in different carbon sources.

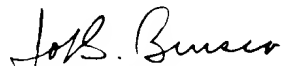
It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of DeRisi et al. by use of probes functionally and structurally equivalent to ESTs that were derived from *Aspergillus oryzae* genes as shown in Machida et al., Minetoki et al., and Hata et al. because Machida et al., Minetoki et al., and Hata et al show the utility of using such probes as a research tool to examine transcription of multiple *Aspergillus oryzae* genes.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4323. The fax phone numbers for the organization where this application or proceeding is assigned are 703 746-5137 for regular communications and 703 746-5137 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-4028.


✓ John S. Brusca
Primary Examiner
Art Unit 1631

jsb
February 21, 2002